



## Review

# Screening, Diagnosis, and Treatment of Patients with Binge Eating Disorder and Obesity: What the Endocrinologist Needs to Know

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**Abstract:** Binge eating disorder (BED) is the most common eating disorder categorized in the DSM-V, but it is often not diagnosed in patients with obesity because it can be difficult to detect in these patients who often have altered eating patterns. In this narrative review, we have highlighted the most recent findings in the screening, diagnosis, and treatment of patients with BED and obesity. The results of our search showed that many BED patients are not obese, and most people with obesity do not have binge behavior. In the diagnostic assessment of these patients, it is important to evaluate not only the clinical and nutritional status and the presence of medical comorbidities, but also the psychological signs and symptoms related to psychiatric comorbidities to define the appropriate diagnosis and the consequent level of treatment. Well-tolerated drugs with action on both body weight and binges can be useful as a second-line complement to cognitive behavioral therapy (CBT). Specific guidelines are needed to obtain consensus on appropriate recommendations in patients with obesity and BED approaching bariatric surgery, taking into account not only weight reduction and clinical data, but also eating behaviors. Identification of BED is important for targeting individuals at high risk of obesity, adverse metabolic patterns, and cardiovascular disease. The challenge is to also achieve lasting weight loss in patients with BED and concomitant obesity.

**Keywords:** binge eating disorder; obesity; treatment; pharmacological therapy; surgery treatment

## 1. Introduction

Binge eating disorder (BED) was included for the first time in the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5)*. It was defined as the presence of “recurrent episodes of binge eating”, characterized by “eating in a discrete period of time, an amount of food that is definitely larger than what most people would eat in a similar period of time under similar circumstances”, associated with “a sense of lack of control over eating during the episode”. The binge-eating episodes are also characterized by “eating much more

*rapidly than normal*", *"eating until feeling uncomfortably full"*, eating large amounts of food without hunger, feeling embarrassed and disgusted with oneself, and eating alone, with a sense of guilt and depression. Other diagnostic criteria are the occurrence of binge eating *"at least once a week for three months"* and not associated with compensatory behaviors as in Bulimia Nervosa (BN). The changes in diagnostic criteria regarding BED, previously categorized in the DSM IV as *"eating disorder not otherwise specified"*, would improve the capacity of clinicians to recognize this disorder in their patients [1]. BED is often associated with overweight and obesity, metabolic syndrome (MS), and diabetes mellitus (DM), but also occurs in people without obesity. BED is more frequently associated, as observed also in Night Eating Syndrome (NES), with psychological and mood disorders compared to patients with similar weight but without disordered eating. BED is more common in women (3.5%) than in men (2%) and in people with obesity (5% to 30%) [2], particularly in those trying to lose weight. The onset of the disease is more frequent in early adulthood, but the prevalence among adolescents continues to increase [2].

The COVID-19 pandemic has exerted a negative effect on the prevalence rates of eating disorders (EDs), their symptoms, psychiatric comorbidity, and the need for care, but the range and the magnitude of this effect is still unknown. Indeed, many results suggest that the COVID-19 pandemic was associated with a widespread negative effect on EDs in patients and in the general population [3]. A systematic review synthesizes the impact of the COVID-19 pandemic on BED new onset and course, in particular after the introduction of restrictive measures to reduce the infection (lockdown), confirming its negative impact [4].

Many risk/protective factors were considered for the new onset of BE symptoms: having an associated mental disorder, the presence of pandemic-associated worry, self-reported pandemic-related loneliness, being female, and belonging to an ethnic minority were all identified as risk factors for the onset or exacerbation of BED [5]. Studies showed that depressive symptoms promoted the development or the worsening of BED and confirmed the increased risk of developing BED during social distancing in people with overweight/obesity as well as in normal-weight adults [6]. The COVID-19 pandemic and related lockdowns are considered a traumatic event, which has promoted dysfunctional eating behaviors, also involving healthcare providers, and affecting therapeutic alliance, due to social distance [7].

Although today BED is the most common eating disorder, many patients are not diagnosed, and some studies report that clinicians can underdiagnose BED, as revealed in a survey [8] where, among respondents who met the diagnostic criteria for BED, only 3.2% had a diagnosis by healthcare providers. Although most people with obesity do not have binge episodes and many patients with BED are not affected by obesity, it is difficult for clinicians to consider BED as a distinct condition from obesity; this represents one of the largest obstacles to the recognition and treatment of this disorder.

The aim of this manuscript is to assist endocrinologists in identifying BED in patients with obesity, targeting individuals at high risk of adverse metabolic and psychological patterns, and defining the appropriate level of treatment.

## 2. Methods

For this narrative review, articles published from 1999 up to 2023 that examined BED, obesity, and their correlations in adults were included. An electronic search was performed using the PubMed database, searching the published literature using the following keywords: *"binge eating disorder"* and *"obesity"* and *"treatment"* and *"bariatric surgery"*. Among the approximately 1200 articles found, guidelines, systematic reviews, meta-analyses, randomized clinical trials, and retrospective studies were included; case reports were excluded. Articles in which the main psychiatric disorder was not BED were excluded; papers in which the main medical condition was not obesity were excluded. Cited articles were selected on the basis of their topicality, relevance, English language, and publication in peer-reviewed journals.

### 3. Diagnosis

The diagnostic assessment is, perhaps, the most important and delicate moment of the entire treatment pathway since it guides the structuring of a therapeutic project inspired by criteria of appropriateness and effectiveness. In this phase, usually carried out on an outpatient basis, the patient should be evaluated at a clinical, nutritional, and psychological level, in order to formulate a diagnosis of state regarding the eating disorder, to evaluate any associated clinical and psychiatric comorbidities, and define, accordingly, the most appropriate level of treatment.

Although a multidisciplinary team is recommended for diagnosis and management, this is not always possible, especially in peripheral hospitals where patients with obesity are dealt with only by endocrinologists. Suggestions for practicing endocrinologists for a quick outpatient evaluation of the presence of BED are therefore important. When should patients be referred to a second-line specialist (psychologist or psychiatrist)? How should a tentative rapid screening be performed? What are the clinical clues raising suspicion for BED?

After inclusion in the DSM-V as a specific disease, with empirical and clinical consistency of diagnostic criteria, other core psychopathologic features, like body and weight overvaluation, may be of clinical and prognostic relevance, and they can be used as markers for diagnosis [9]. In patients with BED, we can find a polarization of thoughts on weight control, diet and binge-avoidance, worse eating control, higher fear of weight gain, and higher body-shape dissatisfaction than non-BED patients with obesity, lower than in BN subjects [10]. Overvaluation of shape and weight can be considered in the severity rate and outcome, in treatment choice, and it would be a specific target for psychological therapies [11]. Food intake patterns are clinically important in BED: they are connected to negative emotions, working as a strategy for managing negative emotions, and are sometimes consequent to excessive diet restrictions that can trigger bingeing [12].

Individuals with obesity and comorbid eating disorders have higher BMIs, a more severe level of depression and obsessive–compulsive symptoms, feeling of inadequacy, and they are at high risk of several medical and psychosocial complications [13]. Stigma and negative biases associated with psychiatric disorders, in patients with BED, are also aggravated by negative weight-based stereotypes and internalized, leading them to feel shame and believe that clinicians do not have time to discuss with them about eating habits and they perceive them to be judgmental about weight problems [14]. In a study on obese patients with and without BED, a negative attitude towards obesity significantly correlated with depression [15]. Other psychiatric comorbidities are mood disorders in 46%, impulse control disorders in 43%, substance use disorders in 23%, personality disorders in 29%, and borderline, obsessive–compulsive personality disorders are found in 10% [16]. Increasing evidence is emerging that an earlier onset of bingeing seems to predict a worse outcome and to require more complex interventions. In addition, data showed that it tends to be a stable syndrome, with a relative stability of binge-eating patterns and lower crossover rates than other eating disorders [17].

In the assessment of BED, clinicians have many screening instruments, like specific questionnaires, to recognize and treat the eating disorder and not only comorbidities. To diagnose BED, clinicians must consider that it is different from simply overeating. At the beginning of the diagnostic–therapeutic pathway, it is advisable to carry out (1) a careful personal and familiar anamnesis (focused both on food behaviors and on any psychiatric comorbidities); (2) an assessment of nutritional status and organic conditions, including the need for laboratory tests depending on the physical condition of the subject; (3) a psychiatric examination considering with special attention the possible risk of suicide and/or self-injurious behavior; and (4) an evaluation of the family and its possible involvement in the course of care (especially for adolescents) [18]. In the case of minors, the assessment must necessarily include the family; for adults, it is highly desirable that the family and/or partner be included. There are currently no standardized tools to assess motivation for treatment.

The diagnosis is multidisciplinary and shared among the various professionals. The professional figures who must therefore participate in the assessment process and who carry out the diagnostic tests, necessary, at this stage, are the psychiatrist, internist, endocrinologist, clinical psychologist, and nutritionist [18]. In consideration of the particular psychopathological characteristics and complexity of the disorder, the importance of the first contact with the patient to establish a good therapeutic relationship appears fundamental. It is also crucial, from the first contact, to guarantee the integration of the medical and psychological areas of evaluation [19].

The medical diagnostic protocol should include clinical–anamnestic evaluation, physical examination, fasting blood glucose, serum lipid profile (total, HDL, and LDL cholesterol, triglycerides), uric acid, thyroid function, liver function (hepatic enzymes), serum creatinine, and cardiovascular assessment [20]. The assessment of nutritional status includes anthropometric evaluations (BMI and waist circumference), assessment of body composition if available (bio-electrical impedance analysis), and body weight history.

It is also necessary to have an evaluation of the eating behavior and a careful qualitative–quantitative nutritional history through the description of eating habits with particular regard to triggering events (emotional state, hunger score), quantitative and qualitative structuring of the meal, investigation of the use of dysfunctional behaviors such as strict dieting, excessive physical activity, binge eating, compensatory behaviors (self-induced vomiting, laxatives, diuretics, various drugs), obsession with food and body forms, insufficient fluid intake with semi-fasting, and psychopathological and psychodiagnostics evaluation [19].

The need to accurately investigate the psychological symptoms and eating habits of the patient who tends to deny their own problem may require the use of structured or semi-structured interviews. The most accredited questionnaires are 1. EAT-40—Eating Attitudes Test [21] of Garner (Italian version validated by M. Cuzzolaro and A. Petrilli in 1988) [22]; 2. EDE 12.OD—Eating Disorders Examination [23] (Italian version validated by V. Ricca) [24]. In the semi-structured interview, the meeting is managed by the therapist who marks the times, contents, and developments, asking the patient specific questions about the history of weight, eating habits, and attitudes regarding body experience, the meaning of the symptom in the psychological history of the patient, and the structuring of the patient's personality. Since patients with EDs often deny or underestimate their symptoms, brief contact with family members, with the attending physician or in any case with a contextual figure, is necessary in the collection of the first information.

The evaluation of the psychopathological characteristics of EDs in adolescence and pre-adolescence must be carried out with specific tools, among which the most recognized are (1) EDE—Eating Disorder Examination, for the evaluation of behavioral and psychological traits related to EDs [23]; (2) CBCL—Child Behavior Checklist, for the evaluation of psychopathological symptoms and psychiatric comorbidity [25]. Since the family represents a resource and an integral element in the treatment of these pathologies, the quality of the relationships that children and adolescents have with their parents is observed, highlighting parental behaviors and attitudes such as the attitude to care, affections, sensitivity, cooperation, availability, indifference, rejection, and control.

The exploration of family dynamics is very important, especially for minors and patients living with the family. This is not only in the case of young patients who still live within the family, but also in adult patients with BED (or other partial disorders). It is also necessary to investigate the family history with respect to psychiatric disorders, alcohol or substance abuse disorder, obesity, family interactions with respect to the disorder of the subject, and family attitudes towards nutrition, exercise, and physical fitness, as well as to identify family stressors that can favor or hinder healing.

#### 4. Metabolic Implications

Both binge eating and obesity are heritable conditions, and BED seems to be partially caused by genetic factors independent of obesity, as observed in a population-based sample

of 2163 female twins evidencing only a modest overlap in the genetic risk factors that increase liability to each condition, considering genetic factors independent of obesity [26]. BED is independently associated with numerous medical comorbidities (including MS, DM, hypertension, dyslipidemias, sleep problems/disorders, pain conditions, asthma, gastrointestinal symptoms/disorders, and among women, menstrual dysfunction, pregnancy complications, polycystic ovary syndrome) [27]. Abraham et al., in the large population-based cohort of the Framingham Heart Study, evidenced an association between BED and high risk of metabolic factors (higher odds of hypertension, hypertriglyceridemia, low HDL, insulin resistance and MS, higher fasting glucose levels, increased visceral subcutaneous and liver fat), attenuated after adjustment for BMI, except for fasting glucose, concluding that binge eaters are at high risk of cardiovascular disease [28]. Hudson et al., in a 5-year longitudinal study, evidenced in BED an increased risk (1.7-fold of any component and 2.4-fold of two or more components) of MS, regardless of the presence of obesity alone [29].

Already in childhood, the presence of BED predicts the development of MS approximately 5 years later, making researching BED in children an important target for treatment [30]. Furthermore, a higher prevalence of BED was seen among NAFLD patients, suggesting a possible connection [31]. Rapid consumption of large amounts of food (often 2000–5000 kcal, ingested in a short time) increases inflammatory and oxidative stress, which is considered an important component for the development of MS, for example, producing rapid and sustained increases in glucose and insulin levels [32]. Research focused on the interactions between BED and gut microbiota: diet seems to be able to modify gut microbiota, facilitating dysbiosis that may produce inflammation, altered gut permeability, causing alterations in the hunger/satiety center, making microbiota a possible target of therapy in BED [33].

Other possible mechanisms in BED seem to involve impaired adipocytokines secretion, leading to higher fasting glucose, such as an insufficient post-prandial leptin production and reduced levels of adiponectin [34,35]. Also, incretin dysregulation, probably due to the eating behavior, is involved in BED: both lower ghrelin pre-meal levels, which may be due to a downregulation by habitual overeating, and a slightly smaller post-meal decline in ghrelin levels contribute to overeating providing a weaker satiety signal [36,37].

#### *Psychotherapeutic Approaches*

Therapy of EDs must necessarily be divided into different levels of treatment (APA, 2006; [1] NICE, 2004 [38]), which are as follows:

- Outpatient regimen;
- Rehabilitation regime (residence and DH—the wording refers to semi-residentiality or day care center and not to hospital DH);
- Hospitalization regime (acute).

These levels are not overlapping or disarticulated, but each represents the most suitable and appropriate response to be used based on what the therapists have evaluated in the assessment phase. Depending on the progress or the peculiar problems that can occur during the therapeutic path, the patient can pass from one level to another. The transition from one level of treatment to another, in the absence of a mandatory sequentiality, is the rule within a personalized care path based on an integrated and interdisciplinary therapeutic approach, which can last up to several years. It is necessary, anyhow, to consider that the transition from one level to another is a particularly delicate moment whether the intensity of the treatment is increased or vice versa, in which the patient is at high risk of destabilization and therefore it is very frequent that drop-out phenomena occur. Furthermore, patients usually do not seek treatment, because of the sense of shame for their eating behavior, and they instead attempt to resolve their medical and psychological issues by themselves, also leading clinicians to focus on comorbidities, delaying treatment for BED. The treatment of comorbidities has little effect without the recognition and treatment of BED, which could also be exacerbated by some medications, particularly those for mood and anxiety disorders that can stimulate appetite [39].



In BED patients, food intake is often related to mood fluctuations, which should be taken into account to manage dietary and behavioral strategies to achieve therapeutic goals [40]. Loss of control is a core feature associated with severe depression, greater body dissatisfaction, and poorer related quality of life.

Eating impulsiveness can be triggered by the restriction of palatable foods and has been related to the hypothesis of a “hedonic deprivation”, where eating impulsiveness can be triggered by restrictions on palatable foods and linked to neurobiological mechanisms similar to those of substance abuse. The “food dependence” is an important correlate of this finding, with dopamine, serotonin, and endogenous opioid systems playing a role in this regard [12]. Patients with BED show an increased reward sensitivity towards food and increased rash-spontaneous behavior, thus shaping a phenotype of obesity with increased impulsiveness, which should be identified and confronted by specific psychological or pharmacological treatments [11].

BED should also be differentiated from other obesity-related eating patterns characterized by eating impulsiveness, not yet recognized as autonomous syndromes, like snacking (introduction of small amounts of food throughout the day), emotional overeating (eating in response to intense emotional states), and selective cravings (intense desire and consuming of specific foods, e.g., sweet eating). These dysfunctional eating behaviors could be considered as subtypes of binge eating; however, their clinical implications have yet to be defined [14].

Individuals with obesity and comorbid EDs are at higher risk of medical and psychosocial complications than individuals with only one of these conditions, and the best long-term treatment strategy has the primary goal to correct binge behavior, alongside a sustainable weight loss [15], also targeting the increase in and maintenance of motivation, the reduction in drop-out rates, and the management of relapses [41]. The treatment combinations need a rising intensity of intervention tailored to the disease severity [42].

Psychotherapeutic approaches to BED, based on cognitive behavioral therapy (CBT) models, are recommendable as first-line treatments and effective on eating behaviors but with unclear results on weight loss [43]. Other simpler psychoeducational interventions and self-help treatments have shown significant efficacy in patients with lower disease severity and less comorbidity [44]. Among the available treatments to be included are CBT, interpersonal psychotherapy, and selective serotonin reuptake inhibitors (SSRIs), with the aim to reduce binge-eating frequency, improve metabolic health and weight, and regulate mood [42]. The APA guidelines recommend a team approach including psychiatrists, psychologists, dietitians, and social workers.

## 5. Drugs Overview

Despite psychological and behavioral therapy being considered the first-line treatment, pharmacotherapy could be one of the possible second-line treatments for BED [45]. The matter is if drugs used for BED can also be effective for comorbid obesity and, vice versa, if drugs used to treat obesity can also be effective in obese people with comorbid BED (Table 1). Several off-label medications have been studied over time, in the attempt to find an effective treatment for BED and its comorbidities, including antidepressants, anticonvulsants, and anti-obesity agents, but to date, the only on-label drug for the treatment of BED, approved by the FDA in 2015, is Lisdexamfetamine dimesylate (LDX) [46]. In this narrative review, drugs that are no longer available because of safety concerns are not discussed.

Antidepressant drugs appear to have positive effects on body weight, but they have not shown incontrovertible advantages in the long-term treatment of BED [47].

Many specialists consider the off-label topiramate, an anticonvulsant approved for the treatment of epilepsy since the 1990s, as a promising second-line therapy for BED, since it is able to reduce both binges and weight, although limited tolerability may arise due to adverse drug reactions [48]. A recent meta-analysis of available randomized clinical trials observed that topiramate was able to reduce the number of binge episodes per week, the number of binge days per week, and the body weight with respect to placebo. However,

topiramate users discontinued treatment for safety reasons more frequently than placebo participants [49].

**Table 1.** Overview of currently approved drugs (FDA/EMA) in the treatment of BED and/or obesity.

Drugs	Approved for BED	Approved for Obesity	Approved for Both
LDX *	+	—	—
ORL * <sup>◦</sup>	—	+	—
NB * <sup>◦</sup>	—	+	—
LIR * <sup>◦</sup>	—	+	—
SEMA * <sup>◦</sup>	—	+	—
PHEN/TPM-ER *	—	+	—

LDX: lisdexamfetamine dimesylate; ORL: orlistat; NB: Naltrexone and Bupropion sustained release; LIR: liraglutide; SEMA: semaglutide; PHEN/TPM-ER: phentermine/topiramate extended release. \* FDA approved; <sup>◦</sup> EMA approved.

### 5.1. Drug Therapy Approved for BED and Their Effects in BED Patients with Obesity

Lisdexamfetamine dimesylate (LDX) is the first on-label treatment for BED in adults ( $\geq 18$  years) but is not indicated for weight loss. It is a pro-drug of d-amphetamine first approved in 2007 by the FDA for the treatment of attention-deficit/hyperactivity disorder (ADHD). After oral administration, LDX is absorbed from the small intestine by active transport via the oligopeptide transporter peptide 1. In the erythrocyte cytosol of the blood cells, LDX undergoes enzymatic hydrolysis of the peptide bond between L-lysine and LDX, thus producing the pharmacologically active d-amphetamine and L-lysine as a by-product. D-amphetamine is metabolized by CYP2D6 and excreted primarily via the kidney. Plasma d-amphetamine has a more advantageous pharmacokinetic profile than an equivalent dose of immediate-release d-amphetamine, due to a lower C<sub>max</sub>, an extended T<sub>max</sub>, and a lower inter- and intra-individual variability. D-amphetamine is able to cross the blood–brain barrier to increase central noradrenergic, dopaminergic, and serotonergic neurotransmission, which could produce a combination of effects on appetite/satiety, reward, and cognitive processes, including attention and impulsivity/inhibition [50,51]. The efficacy of LDX in the treatment of moderate to severe BED has been demonstrated in many studies, indicating that LDX is able to reduce overall binge-eating episodes and symptoms such as severity and obsessive–compulsive and impulsive characteristics of the BED [52]. Evaluating the maintenance of efficacy of LDX therapy, a multicenter, double-blind, placebo-controlled, randomized clinical trial evidenced that continued LDX treatment is associated with a significantly lower risk of relapse for binge eating at 6 months, compared to placebo (3.7% vs. 32.1%). Participants' BMI was 18 to 45 kg/m<sup>2</sup> at baseline, but it should be noted that they were predominantly female, white, and affected by obesity.

LDX adverse events reported by more than 5% of participants were mostly mild or moderate (dry mouth, headache, insomnia, nasopharyngitis, upper respiratory tract infection), and only two serious: breast cancer and nerve root. Furthermore, although the study did not include pregnancies, an unexpected pregnancy and the death of the infant born with exomphalos, limb malformation, and congenital diaphragmatic hernia were reported. An increase in blood pressure and heart rate was noted, such as a decrease in body weight (mean  $\pm$  SD:  $-8.29 \pm 7.62$  kg in LDX;  $-4.25 \pm 5.29$  kg, in placebo group) [53]. Currently, LDX has no indications for weight loss, mainly for the greater cardiovascular risk associated with obesity. Cardiovascular safety information from BED clinical trials is limited, given the exclusion of patients at higher risk (e.g., persons with diabetes, moderate to severe hypertension, and cardiovascular disease), so LDX should not be used in patients with symptomatic cardiovascular disease, nor in patients with moderate to severe hypertension who use other sympathomimetic drugs or who have a family history of sudden/cardiac death and should be used with caution in patients who are involved in strenuous physical activity.

In another systematic review and meta-analysis, a greater efficacy of LDX than placebo in reducing binge days per week, BED-related obsessive-compulsive symptoms, weight, and remission rates was observed, although discontinuation rates were higher for LDX than for placebo [54]. Further information is awaited from an ongoing registered clinical trial (ClinicalTrials.gov identifier: NCT03924193) testing the usefulness of combining LDX with CBT to evaluate the efficacy of a combined approach for BED patients with comorbid obesity.

## 5.2. Drugs Approved for Obesity and Their Effects in Obese Patients with BED

Numerous drugs are currently approved as an adjunct to a reduced-calorie diet and increased physical activity in adults with obesity ( $\text{BMI} \geq 30 \text{ kg/m}^2$ ) or overweight with  $\text{BMI} \geq 27 \text{ kg/m}^2$  in the presence of at least one weight-related comorbidity (such as hypertension, Type 2 diabetes, or dyslipidemia), but they are not approved for the treatment of BED [55,56]. Many studies have explored the effects of orlistat, a lipase inhibitor that produces a dose-dependent reduction in the absorption of dietary fat, as an adjunct to CBT, with several conflicting results. Some authors have observed greater weight loss than adding placebo to CBT, in the presence of comparable improvements in the eating disorder, considering orlistat an opportunity to treat patients with obesity and BED [57]. Others observed that adding orlistat to behavioral weight loss produced a greater weight loss than placebo among obese patients without BED, but not among those with BED [58]. Overall, orlistat, even in the long-term, did not appear to adversely affect eating behavior, compared to placebo, during a behavioral program [59].

The combination of Naltrexone and Bupropion sustained release (NB), which works by stimulating POMC neurons (bupropion) as well as blocking endogenous feedback that inhibits POMC activity (naltrexone), acting on hypothalamic and reward circuits, has been proven to be an effective therapy for weight loss in patients with obesity [60–62]. Carbone et al., in an open-label trial, compared patients with BED and obesity with a control group of patients with obesity without BED treated with NB for 16 weeks in addition to a low-calorie diet and increased physical activity. They observed an improvement in pathological eating behavior and a significant and similar weight loss ( $\Delta \text{BMI}\% \approx 8\%$ ) in both groups, concluding that NB appear to be an effective and well-tolerated option for weight loss in patients with obesity and BED [63]. In a recent placebo-controlled double-blind pilot randomized control trial, Grilo et al. evaluated the effects of 12 weeks of NB or placebo in persons with BED and obesity ( $\text{BMI} 30\text{--}50 \text{ kg/m}^2$ ), also evaluating the long-term effects through a 6-month follow-up after therapy discontinuation. They observed significant reductions in binge eating, eating disorder psychopathology, depression, and weight during treatment, without significant differences between NB and placebo, although the proportion of patients achieving 3% weight loss was significantly greater with NB than placebo (45.5% vs. 0%) and weight loss and reductions in bingeing were significantly correlated in the NB group. At 6-month follow-up, the results remained improved from baseline, with no significant differences between NB and placebo and no significant differences were reported in adverse events [64]. The efficacy of NB (compared to placebo) in weight reduction in BED patients with and without obesity was confirmed, with the obesity status not predicting or moderating therapeutic outcomes [65].

The results of the randomized double-blind placebo-controlled study NCT03045341 were recently published. This study tested NB and BWL therapy, alone and in combination, in 136 patients with BED and obesity (81.6% women, mean age 46.5 years, mean BMI  $37.1 \text{ kg/m}^2$ ). Binge-eating remission rates were 17.7% in the placebo group, 31.3% in the NB group, 37.1% in the BWL + placebo group, and 57.1% in the BWL + NB group. BWL was significantly superior to no BWL, and NB was significantly superior to placebo, but no significant interaction was found between BWL and medication. The 5% weight loss rates were 11.8% in the placebo group, 18.8% in the NB group, 31.4% in the BWL + placebo group, and 38.2% in the BWL + NB group. The results support the potential efficacy of NB for BED treatment, especially when associated with BWL, which was able to provide superior



improvement on secondary measures (eating disorder psychopathology, depression, eating behaviors, and cholesterol and HbA1c levels) compared with no BWL [66]. Furthermore, adult BED patients with comorbid obesity who have good responses to acute NB treatment have a good maintenance of binge remission, low binge frequency, and significant additional weight loss [67].

Glucagon-like peptide-1 (GLP-1) receptors have been found in central nervous system areas involved in appetite regulation, and GLP-1 receptor agonists (GLP1ras) are able to modulate appetite and reward-related brain areas in humans. Therefore, some authors hypothesized that GLP1ras used for weight loss could have positive effects in BED [68]. The glucagon-like peptide-1 analogue liraglutide (LIR) is approved for obesity in adults and in adolescents from the age of 12 years. In a pilot study, LIR showed a significant improvement in binge eating and a reduction in body weight, BMI, waist circumference, systolic blood pressure, fasting glycaemia, and total cholesterol in obese ( $\text{BMI } 35.9 \pm 4.2 \text{ kg/m}^2$ ) non-diabetic subjects after 3 months of treatment. However, the authors also reported a significant increase in ghrelin levels, highlighting the risk of the drug losing efficacy over time [69]. In combination with intensive behavioral therapy (IBT), LIR was able to produce greater short-term improvements in body weight, dietary disinhibition, global eating disorder psychopathology, and shape concerns than IBT alone [70]. An open-label study examined the effects of semaglutide (SEMA) in individuals with BED, treated with SEMA alone or in combination with lisdexamphetamine or topiramate, with SEMA alone exhibiting greater reductions in BES scores [71].

Phentermine/topiramate extended release (PHEN/TPM-ER) is another drug used for the treatment of obesity; it is an oral combination of phentermine hydrochloride, an appetite-suppressant sympathomimetic amine, and topiramate, an anti-epileptic medication [72]. PHEN/TPM-ER was shown to be safe and well tolerated with low discontinuation rates in adults with obesity, and recently, the FDA approved it for chronic weight management in patients with obesity aged  $\geq 12$  years [73]. PHEN/TPM-ER in a 12-week, open-label, prospective study was found to be well tolerated and effective in reducing body weight ( $-4.9 \pm 1.2 \text{ kg}$ ), BMI, and binge-eating symptoms in individuals with BED and obesity or overweight [74]. In a randomized, placebo-controlled crossover trial, in 22 adults with obesity ( $\text{BMI } 31.1 \pm 6.2 \text{ kg/m}^2$ , female 96%, aged  $42.9 \pm 10.1$  years) predominantly with BED and 4 with BN, 12 weeks of PHEN/TPM-ER treatment was shown to be well tolerated and significantly more effective than placebo in reducing binge eating and weight ( $-5.8 \text{ kg}$ ; placebo  $+ 0.4 \text{ kg}$ ) [75].

## 6. Bariatric Surgery Overview

Higher rates of EDs are reported in bariatric surgery candidates, and BED is the most common in pre-operative prevalence rates, with a wide range due to different assessment methods and study designs, including variation in the DSM-5 criteria, ranging at 17% in a recent meta-analysis [76,77]. At present, BED is no longer considered a contraindication for access to bariatric surgery, as long as a targeted specialist framework and a multidisciplinary assessment are made, with possible psychotherapeutic treatment and intervention on proper nutrition education, focused on the normalization of eating patterns and improvement in mood, providing there is strict monitoring before and after surgery by an interdisciplinary team [78–81].

Numerous studies revealed conflicting results about the relationship between the presence of BED and post-bariatric surgery weight loss, revealing poorer effects [82,83], or also no relationship in the long-term [77], probably due to the different study methodology. A recent study suggested that bariatric surgery improves food addiction symptomatology, but subjects in whom food addiction persisted after bariatric surgery likely have a more severe form that is characterized by greater binge-eating characteristics and psychosocial distress that may improve with cognitive behavioral therapy [84].

The post-operative reduced gastric capacity objectively limits the amount of food ingested at one time, so it is certainly difficult to determine what is the definition of the

“large” amount of food eaten. Existing diagnostic and standard criteria may be insufficient to reveal the atypical presentations in post-operative patients, making it necessary to develop appropriated screenings and internationally validated measures [85]. Furthermore, after bariatric surgery, shape concerns are frequent, as after weight loss, there is loose skin and impairment caused by excessive skin that may produce greater body dissatisfaction and depressive mood in these patients [86]. Kruseman et al. evidenced that 8 years after gastric bypass, more than half of the patients obtained a successful weight loss (59%), but a disordered eating behavior (BED or NES) was also frequent (51%) [87]. Indeed, problematic eating behaviors appear to be associated with a worse outcome after bariatric surgery [88]. Kofman et al. also evidenced greater weight regain, lesser excess weight loss, and poorer health-related quality of life correlating with frequency of binge eating as risk factors for diminished weight outcomes after gastric bypass [89].

All these data evidenced the importance of close monitoring after surgery to reveal post-operative re-emerging disorders, as well as new eating disorders, in a long-term follow-up. Table 2 summarizes what is detailed in the work (Table 2).

**Table 2.** Relevant points to consider in the treatment of BED in obesity and in the treatment of obesity in BED.

	Key Points in the Treatment of BED in Obesity	Key Points in the Treatment of Obesity in BED
Diagnosis	Clinicians dealing with BED must also pay attention to the presence of obesity and its metabolic complications.	Clinicians dealing with obesity and their metabolic implications must also pay attention to the presence of BED.
Treatment	Psychotherapeutic approaches: CBT models, psychoeducational interventions or self-help treatments, interpersonal psychotherapy. A team approach including psychiatrics, psychologists, endocrinologist, dieticians, and social workers is recommended.	A team approach including endocrinologist, dieticians, psychiatrists, psychologists, and social workers is recommended to set up an adequate approach in obese patients in whom BED is also diagnosed.
On-label therapy	LDX is the first on-label treatment for BED in adults, but is not approved for weight loss.	Many drugs are intended for adults who are obese or overweight with at least one weight-related factor, but they are not approved for treating BED.
Bariatric surgery	BED is common in BS candidates. Currently, BED is no longer considered a contraindication, provided that rigorous multidisciplinary monitoring is carried out before and after BS.	BED may flare up or appear de novo after BS. Careful monitoring is required in long-term multidisciplinary follow-up.

BED: binge eating disorder; CBT: cognitive behavioral therapy; LDX: Lisdexamfetamine dymesilate; BS: bariatric surgery.

7. Conclusions

Screening of BED is important for targeting individuals at high risk of weight gain, adverse metabolic patterns, and cardiovascular disease. On the other hand, in patients suffering from obesity who therefore present an increased cardiovascular and metabolic risk, the presence of BED must be sought and treated to improve therapeutic outcomes. It is important to recognize both of these conditions in patients, to improve both pathologies. Today, we have useful tools to cure them, with different levels of treatment.

Cognitive behavioral therapy remains the mainstay treatment. New drugs designed to treat BED, such as LDX, could offer good hope even in patients with concomitant obesity.

The drugs used to treat obesity, and especially NB, also seem to offer good prospects for the treatment of patients with obesity suffering from BED.

Even bariatric surgery, often considered contraindicated in patients with BED, is now feasible in patients evaluated and followed by a multidisciplinary team.

Although the creation of well-tolerated treatments capable of simultaneously treating both BED and obesity is still necessary, certainly the multidisciplinary approach, which includes different figures trained in the sector, is desirable for the best treatment. The definition of a positive outcome should take into account not only weight reduction and clinical data, but also improvement in problematic eating behaviors.

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